中 山 醫 學 大 學 附 設 醫 院

甲 狀 腺 癌 診 療 指 引

本臨床指引參考國家衛生研究院、與美國NCCN版本

甲狀腺癌多專科醫療團隊編修

甲狀腺癌治療指引制訂日期

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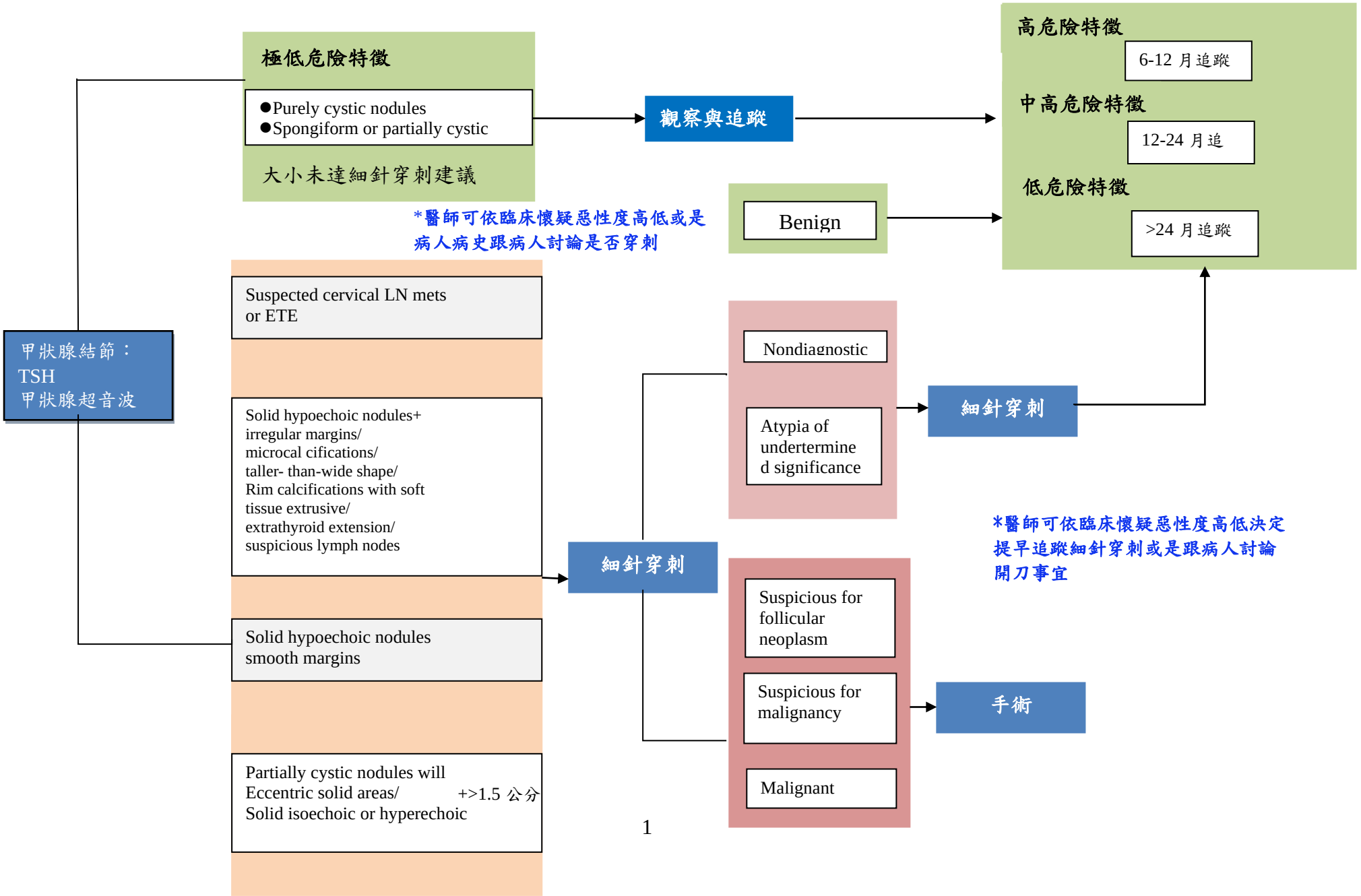
癌症委員會主任委員	癌症委員會執行長	癌症中心主任	團隊負責人

修訂內容

頁數	原文	修訂/增修
	定期檢閱	無修訂

目　　錄

一、甲狀腺結節


甲狀腺結節：
TSH
甲狀腺超音波
極低危險特徵
●Purely cystic nodules
●Spongiform or partially cystic
大小未達細針穿刺建議
觀察與追蹤
高危險特徵
6-12 月追蹤
中高危險特徵
12-24 月追
低危險特徵
>24 月追蹤
Benign
*醫師可依臨床懷疑惡性度高低或是病人病史跟病人討論是否穿刺
Suspected cervical LN mets or ETE
Solid hypoechoic nodules+ irregular margins/ microcal cifications/ taller- than-wide shape/ Rim calcifications with soft tissue extrusive/ extrathyroid extension/ suspicious lymph nodes
Solid hypoechoic nodules smooth margins
Partially cystic nodules will Eccentric solid areas/ Solid isoechoic or hyperechoic
+>1.5 公分
細針穿刺
Nondiagnostic
Atypia of undetermined significance
細針穿刺
Suspicious for follicular neoplasm
Suspicious for malignancy
Malignant
手術
*醫師可依臨床懷疑惡性度高低決定提早追蹤細針穿刺或是跟病人討論開刀事宜

二、甲狀腺癌術前評估

一般術前評估：

胸部 X 光
心電圖
一般血液學
肝、腎功能檢查

＋

甲狀腺癌術前評估：

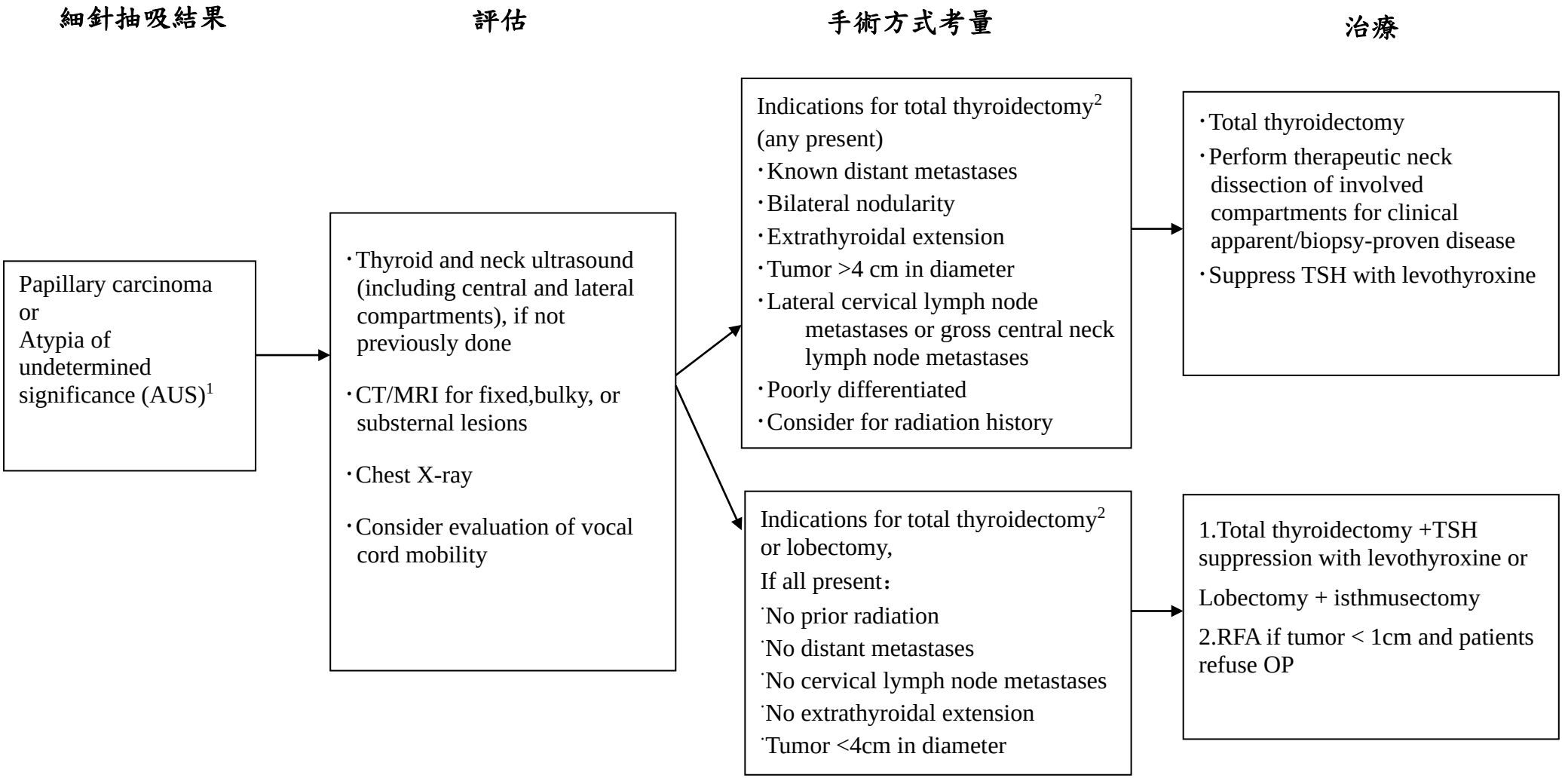
頸部超音波 ＋ 淋巴結評估

***選擇性**

-頸部 CT 或 MRI
-B、C 型肝炎檢查
-會診 ENT 看聲帶功能(如：頸部手術過)

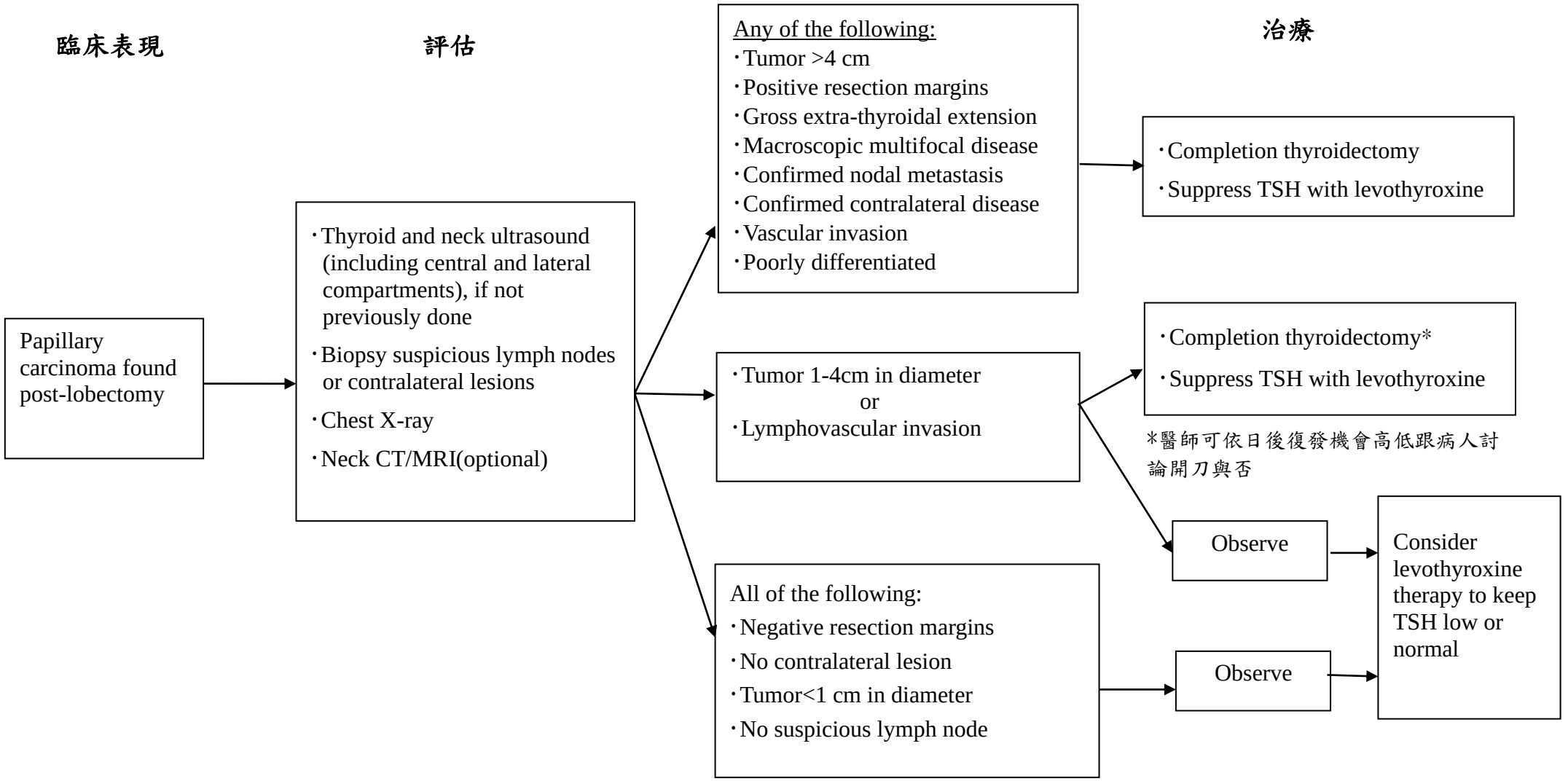
三、手術治療方式

1. 乳突癌（Papillary Carcinoma）

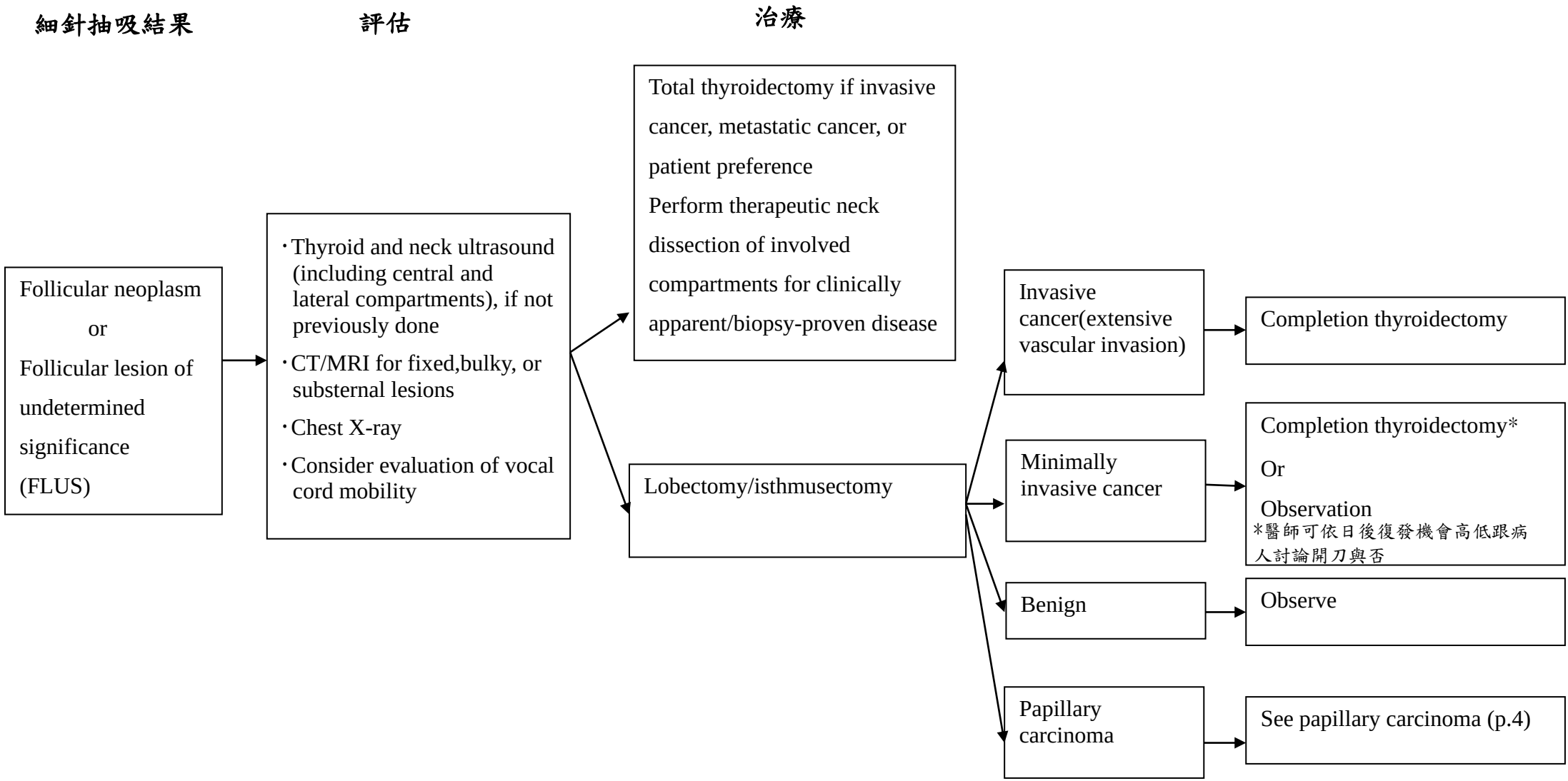


[1]AUS with high clinical suspicion of malignancy may consider lobectomy or total thyroidectomy for definitive diagnosis/treatment
[2]For those who underwent total thyroidectomy, lesion site lobectomy with frozen section might be considered

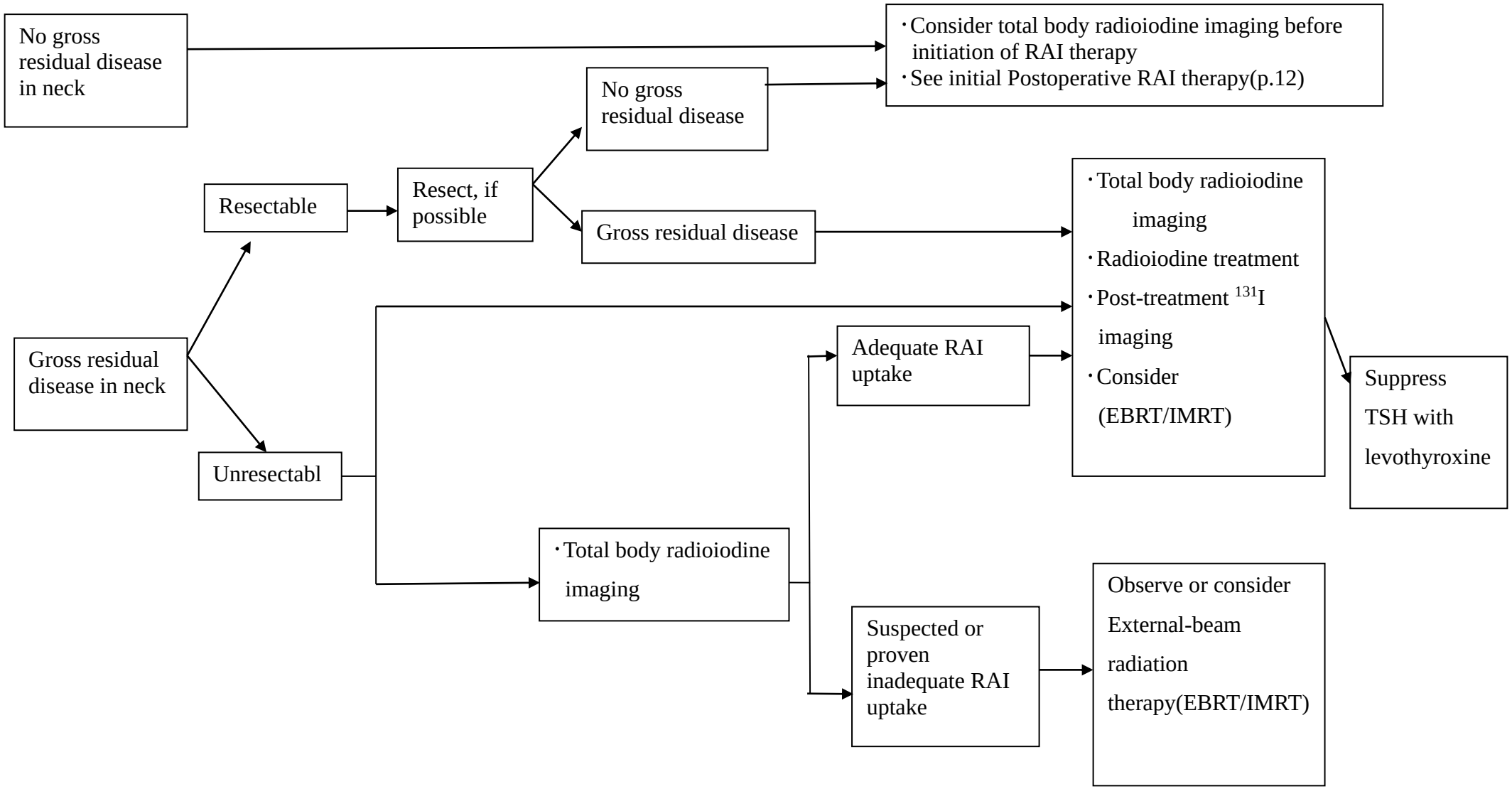
2. 術前認為良性之病灶，作單葉切除術後確認為乳突癌(Papillary carcinoma found post-lobectomy)



3. 濾泡癌（Follicular Carcinoma）



四、術後評估與治療


No gross residual disease in neck
・Consider total body radioiodine imaging before initiation of RAI therapy
・See initial Postoperative RAI therapy(p.12)
No gross residual disease
Resectable
Resect, if possible
Gross residual disease
・Total body radioiodine imaging
・Radioiodine treatment
・Post-treatment 131I imaging
・Consider (EBRT/IMRT)
Suppress TSH with levothyroxine
Gross residual disease in neck
Unresectabl
Adequate RAI uptake
・Total body radioiodine imaging
Suspected or proven inadequate RAI uptake
Observe or consider External-beam radiation therapy(EBRT/IMRT)

五、2015 ATA risk stratification system with Proposed Modifications

Low risk	Papillary thyroid cancer(with all of the following): ・No local or distant metastases; ・All macroscopic tumor has been resected ・No tumor invasion of loco-regional tissues or structures ・The tumor does not have aggressive histology(e.g., tall cell,hobnail variant,columnar cell carcinoma) ・If ^{131}I is given, there are no RAI-avid metastatic foci outside the thyroid bed on the first posttreatment whole-body RAI scan ・No vascular invasion ・Clinical N0 or ≦5 pathologic N1 micrometastases(<0.2cm in largest dimension)[a] ・Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer[a] ・Intrathyroidal,well differentiated follicular thyroid cancer with capsular invasion and no or minimal (<4 foci)vascular invasion[a] ・Intrathyroidal,papillary microcarcinoma,unifocal or multifocal, including BRAF^{V600E}mutated(if known)[a]
Intermediate risk	・Microscopic invasion of tumor into the perithyroidal soft tissues ・RAI-avid metastatic foci in the neck on the first posttreatment whole-body RAI scan ・Aggressive histology(e.g.,tall cell,hobnail variant,columnar cell carcinoma) ・Papillary thyroid cancer with vascular invasion ・Clinical N1 or >5 pathologic N1 with all involved lymph nodes <3cm in largest dimension[a] ・Multifocal papillary microcarcinoma with ETE and BRAF^{V600E}mutated(if known)[a]
High risk	・Macroscopic invasion of tumor into the perithyroidal soft tissues(gross ETE) ・Incomplete tumor resection ・Distant metastases ・Postoperative serum thyroglobulin suggestive of distant metastases ・Pathologic N1 with any metastatic lymph node 3cm in largest dimension[a] ・Follicular thyroid cancer with extensive vascular invasion(>4 foci of vascular invasion)[a]

BRAF (院內代碼 2502011 , 自費 3600 元) :
可由 Cytology 或 Pathology 檢體檢驗

[a] proposed modifications, not present in the original 2009 initial risk stratification system

六、術後碘-131治療原則

*需確定為分化良好甲狀腺癌 + 甲狀腺全切除

	定義		*原子碘
低復發	病理報告	**以下需全部符合 All macroscopic tumor has been resected No tumor invasion of loco-regional tissues or structures No aggressive histology(e.g., tall cell,hobnail variant, columnar cell) No vascular invasion Papillary microcarcinoma, unifocal or multifocal, BRAFV6001E mutated **Follicular cancer** Intra-thyroidal, **encapsulated** follicular variant or capsular invasion but no/**minimal (<4 foci)vascular invasion**	小劑量
	N 淋巴結	Clinical N0 or <5 N1 micro-metastases(<0.2 cm)	
	M 轉移	No local or distant metastases	
	治療後碘掃描	No RAI-avid metastatic foci outside the thyroid bed	
中復發	病理報告	Microscopic invasion of tumor into the peri-thyroidal soft tissues Aggressive histology Papillary thyroid cancer with vascular invasion Multifocal papillary microcarcinoma with ETE and BRAFV600E mutated	大劑量 轉介**碘-131** 病房
	N 淋巴結	Clinical N1 or >5 pathologic N1 with all involved lymph nodes <3cm	
	治療後碘掃描	RAI-avid metastatic foci in the neck	
高復發	病理報告	**以下任一符合 Macroscopic invasion of tumor into the perithyroidal soft tissues(gross ETE) Incomplete tumor resection Follicular cancer with >4 foci of vascular invasion	大劑量 轉介**碘-131** 病房
	N 淋巴結	Pathologic N1 with metastatic lymph node >3cm in largest dimension	
	M 轉移	Distant metastases Postoperative serum thyroglobulin suggestive of distant metastases	

六、術後碘-131治療原則(續)

***碘-131 劑量**

小劑量

門診：30mCi for ablation

大劑量

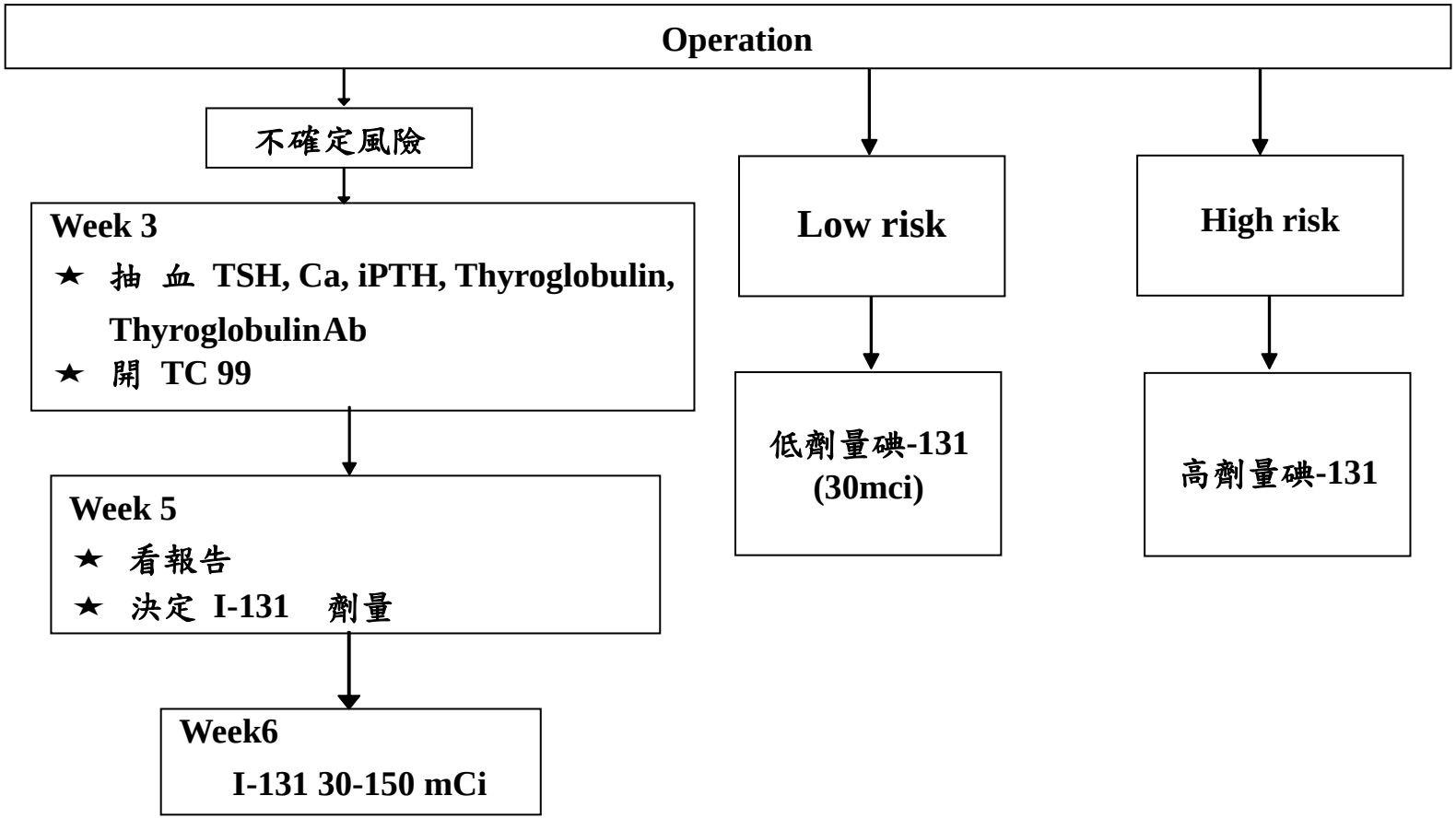
同位素病房：80 mCi,100 mCi,120 mCi,150 mCi,200 mCi

*年紀>70 建議 100-150 mCi

*腎功能不全 建議劑量少一點

*高復發風險 建議 100-200 mCi

CSMUH Post-operation follow-up protocol



考慮排除條件:
Pre-op FDG PET uptake (+)

七、手術及碘-131治療後追蹤

Dynamic risk stratification

	定義		處置建議
Excellent response	Tg(ng/mL) Suppressed：<0.2 − TSH-stimulated：<1 頸部超音波 −	碘-131 全身掃描 ‧不建議用在 ATA low risk − if Tg- sono-	**TSH 目標：** **0.5-2 low-to-intermediate** **0.1-0.5 for high risk**
Biochemical incomplete	Tg(ng/mL) Suppressed：≧1 TSH-stimulated：≧10 + Rising anti-Tg 頸部超音波 −	碘-131 全身掃描 − 正子造影 − *TSH stimulated Tg≧10	**TSH 目標：** **0.1-0.5** **0.5-2 if atrial fibrillation** I^{131} 100-200mci If stimulated Tg>10,碘掃描- 正子造影-
Structural incomplete	Tg(ng/mL) Any TG or 頸部超音波 +	碘-131 全身掃描 + or 正子造影 + *TSH stimulated Tg≧10	**TSH 目標：** **<0.1** **0.1-0.5** **如有心房顫動** **復發或轉移**

八、復發或轉移治療建議

<table>
<tr><td>頸部及淋巴結</td><td>TSH <0.1
0.1-0.5 if 心房顫動
± 手術
If 淋巴結 >0.8-1cm
+ 碘-131*
(RFA if patients refuse to OP)</td></tr>
<tr><td>鄰近氣管消化道</td><td>TSH <0.1
0.1-0.5 if 心房顫動
+ 手術
+ 碘-131*
(RFA if patients refuse to OP)</td></tr>
<tr><td>遠端轉移
腦部
骨頭
肺部</td><td>TSH <0.1
0.1-0.5 if 心房顫動
± 手術
If 只有單處轉移
+ 碘-131*
100-200 mCi
Steroid
Before I^{131}
+ 放射治療
If 多處轉移
100-200mCi
+ 放射治療
100-200mCi
Q6-12m</td></tr>
</table>

*碘-131 治療需患處在碘掃描有顯影

九、碘-131治療無效治療建議

定義	治療建議
1. 病灶不吸收放射性碘 2. 病灶失去原本吸收放射性碘的能力 3. 某些病灶會吸收，某些不會 4. 病灶吸收放射性碘，但疾病仍持續惡化	**甲狀腺素抑制治療** 如病人無症狀，穩定** 病灶在 12 月內長徑增加<20% **局部控制治療** 手術 或 放射治療 或 RFA **標靶藥物(ex:Nexava、Lenvima)** 如病人有症狀，快速進展(<6 個月)，病灶危及生命 *多數骨轉移: 雙磷酸鹽 或 denasumab

**無症狀，病情穩定無惡化的病人可使用甲狀腺素抑制治療為主

十、放射線治療

Differentiated, Medullary, or Poorly Differentiated (non-anaplastic) Thyroid Cancer

- Adjuvant RT for high-risk disease (after R1 resection)
  - Microscopic disease (thyroid bed, involved resected lymph node regions): 60–66 Gy in 1.8–2 Gy per fraction
  - Elective nodal regions: 50–56 Gy in 1.6–2 Gy per fraction
- Salvage RT after R2 resection or inoperable patients
  - Gross disease: 66–70 Gy in 1.8–2 Gy per fraction
  - Microscopic disease (thyroid bed, involved resected lymph node regions): 60–66 Gy in 1.8–2 Gy per fraction
  - Elective nodal regions: 50–56 Gy in 1.6–2 Gy per fraction
- Palliative RT of metastases
  - Bony or soft-tissue metastases[22]
    - For patients with oligometastatic disease and good performance status consider higher doses (45–60 Gy) in 1.8–2 Gy daily fractions, or SBRT following principles for treatment of oligometastases
    - For patients with widely metastatic disease and/or poor performance status limiting life expectancy, consider 8 Gy in 1 fraction; 20 Gy in 5 daily fractions; 30 Gy in 10 daily fractions
  - CNS metastases
    - ≤4 metastases – consider stereotactic radiosurgery (SRS) either following surgical resection or as monotherapy
    - Multiple metastases:
      - Consider enrollment on clinical trial for SRS versus whole brain radiation therapy (WBRT) (with or without hippocampal avoidance)
      - WBRT – 30 Gy in 10 daily fractions; consider 45 Gy in 1.8 Gy daily fractions for good performance status.

Anaplastic Thyroid Cancer

- Adjuvant RT after R0 or R1 resection[14,25-27]
  - Microscopic disease/high-risk regions: 60–66 Gy in 1.2 Gy twice daily fractions or 1.8–2 Gy daily fractions
  - Elective nodal regions can be treated with SIB: 45–54 Gy in 0.8–1.0 Gy twice-daily fractions or 1.6–1.8 Gy once-daily fraction
  - Chemoradiation may be considered on an individual basis.
- Salvage RT after R2 resection or inoperable patients
  - Gross disease: 66–70 Gy in 1.2 Gy twice-daily fractions or 1.8–2 Gy daily fractions
  - Microscopic disease/high-risk regions: 60–66 Gy in 1.2 Gy twice daily fractions or 1.8–2 Gy daily fractions
  - Elective nodal regions can be treated with SIB: 45–54 Gy in 0.8–1.0 Gy twice-daily fractions or 1.6–1.8 Gy once-daily fraction
  - Chemoradiation may be considered on an individual basis.[13]
- Palliative neck RT： 20 Gy in 5 daily fractions, 30 Gy in 10 daily fractions, 45 Gy in 15 daily fractions
- Palliative RT of metastases
  - Bony or soft tissue metastases：8 Gy in 1 fraction; 20 Gy in 5 daily fractions; 30 Gy in 10 daily fractions
  - CNS metastases：Whole brain radiation – 30 Gy in 10 daily fractions

十一、標靶治療處方、化學治療處方及免疫治療處方

標靶治療處方(Kinase Inhibitor Therapy)

Regimen	Agents/Dosages	Frequency
Dabrafenib/trametinib (*BRAF* V600E mutation positive)	Dabrafenib 150 mg PO and Trametinib 2 mg PO	Twice daily Once daily
Larotrectinib (*NTRK* gene fusion positive)	100 mg PO	Twice daily
Entrectinib *(NTRK* gene fusion positive)	600 mg PO	Once daily
Selpercatinib (*RET* fusion positive)	120 mg PO (< 50 kg) or 160 mg PO (≥ 50 kg)	Twice daily
Sorafenib (Nexavar)[a]	400mg Oral	Twice daily
Lenvatinib(Lenvima)[a]	24mg/ Oral	Daily
Vandetanib(Caprelsa)[b]	Max 300mg/ Oral	Daily
Pralsetinib (RET fusion positive)	400mg PO	Once daily

健保規範:

a. 用於放射性碘治療無效之局部晚期或轉移性的進行性(progressive)分化型甲狀腺癌(RAI-R DTC)：
(1)需經事前審查核准後使用，每次申請之療程以 3 個月為限，送審時需檢送影像資料，每 3 個月評估一次。
(2)Sorafenib 與 lenvatinib 僅得擇一使用，不得互換。(109/1/1)

b. 適用於無法進行手術切除的局部侵犯或轉移性甲狀腺髓質癌，並且為症狀性及疾病侵襲性的患者。(109/11/1)
(1)需經事前審查核准後使用，每次申請之療程以 6 個月為限，送審時需檢送影像資料，每 6 個月評估一次。
(2)出現疾病惡化或無法忍受之藥物不良反應，應立即停用。
(3)每日最大劑量為 300 毫克

化學治療處方(Chemotherapy Regimen)Systemic Therapy Regimens for Metastatic Disease

Regimen	Agents/Dosages	Frequency
Paclitaxel	60-80 mg/m^2 IV	Weekly
Paclitaxel	135-150 mg/m^2 IV	Every 3-4 weeks
Doxorubicin or Epirubicin/Pharmarubicin	20mg/m^2 IV 30mg/m^2 IV	Weekly Weekly
Doxorubicin or Epirubicin/Pharmarubicin	60-75 mg/m^2 IV 90-110 mg/m^2 IV	Every 3 weeks Every 3 weeks
Paclitaxel/carboplatin	Paclitaxel 60–80 mg/m2 , carboplatin AUC 2 IV or Paclitaxel 135–150 mg/m^2 , carboplatin AUC 5–6 IV	Weekly Every 3–4 Weeks
Docetaxel/doxorubicin	Docetaxel 60 mg/m^2 IV, doxorubicin 60mg/m^2 IV or Epirubicin 90mg/m^2 (with pegfilgrastim) or Docetaxel 20 mg/m^2 IV, doxorubicin 20mg/m^2 IV or Epirubicin 30mg/m^2 IV	Every 3–4 weeks Weekly

免疫治療處方(Immunotherapy)

Regimen	Agents/Dosages	Frequency
Pembrolizumab (TMB-H [≥10 mut/Mb])	200mg IV or 400mg IV	Every 3 weeks Every 6 weeks

Adjuvant/Radiosensitizing Chemotherapy Regimens - Anaplastic Carcinoma

Regimen	Agents/Dosages	Frequency
Paclitaxel/carboplatin	Paclitaxel 50 mg/m2 , carboplatin AUC 2 IV	Weekly
Docetaxel/doxorubicin	Docetaxel 60 mg/m^2 IV, doxorubicin 60mg/m^2 IV or Epirubicin 90mg/m^2 Docetaxel 20 mg/m^2 IV, doxorubicin 20mg/m^2 IV or Epirubicin 30 mg/m^2 IV	Every 3–4 weeks Weekly
Paclitaxel	30–60 mg/m2 IV	Weekly
Cisplatin	30–35mg/m2 IV	Weekly
Doxorubicin or Epirubicin/Pharmarubicin	20mg/m2 IV or 30mg/m2 IV	Weekly Weekly
Doxorubicin or Epirubicin/Pharmarubicin	60mg/m2 IV or 90mg/m2 IV	Every 3 weeks Every 3 weeks

十二、AJCC 8 edition

Differentiated and anaplastic thyroid carcinoma TNM staging AJCC UICC 2017

Primary tumor (T)

Papillary, follicular, poorly differentiated, Hurthle cell and anaplastic thyroid carcinoma	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤1 cm in greatest dimension limited to the thyroid
T1b	Tumor >1 cm but ≤2 cm in greatest dimension limited to the thyroid
T2	Tumor >2 cm but ≤4 cm in greatest dimension limited to the thyroid
T3	Tumor >4 cm limited to the thyroid, or gross extrathyroidal extension invading only strap muscles
T3a	Tumor >4 cm limited to the thyroid
T3b	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing the carotid artery or mediastinal vessels from a tumor of any size
NOTE: All categories may be subdivided: (s) solitary tumor and (m) multifocal tumor (the largest tumor determines the classification).	

Regional lymph nodes (N)

N category	N criteria
NX	Regional lymph nodes cannot be assessed
N0	No evidence of locoregional lymph node metastasis
N0a	One or more cytologically or histologically confirmed benign lymph nodes
N0b	No radiologic or clinical evidence of locoregional lymph node metastasis
N1	Metastasis to regional nodes
N1a	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian, or upper mediastinal) lymph nodes. This can be unilateral or bilateral disease.
N1b	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (levels I, II, III, IV, or V) or retropharyngeal lymph node

Distant metastasis (M)

M category	M criteria
M0	No distant metastasis
M1	Distant metastasis

AJCC8 *Age at diagnosis for staging increased from 45 to 55

Differentiated thyroid cancer

When age at diagnosis…	*And T is….*	*And N is….*	*And M is….*	*Then the stage group is…*
<55 yrs	Any T	Any N	M0	I
	Any T	Any N	M1	II
≧55yrs	T1	N0/NX	M0	I
	T1	N1	M0	II
	T2	N0/NX	M0	I
	T2	N1	M0	II
	T3a/T3b	Any N	M0	II
	T4a	Any N	M0	III
	T4b	Any N	M0	IVA
	Any T	Any N	M1	IVB

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十四、甲狀腺癌完治定義

癌別	期別		治療方式	完治定義
甲狀腺癌	治療期	1 期 2 期 3 期	OP	手術(單邊)→完治 手術(兩側全切)，I-131+抽血(Thyroglobulin+Thyroglobulin-Antibody)，若無復發的證據→完治。
		4 期	OP OP→I-131 標靶 C/T	1.如有手術，手術後接受輔助性治療算完治 2.未手術，口服標靶藥物 or 化學治療三個月即算完治 3.治療中轉安寧療護算完治